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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/558,472	04/25/2000	Michael R. Bristow	MYOG:004DIV1	8819

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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	12

DATE MAILED: 03/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/558,472	BRISTOW ET AL.	
	Examiner	Art Unit	
	Thai-An N. Ton	1632	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 April 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' Amendment, filed 1/13/03, Paper No. 11, has been entered. Claim 23 has been amended.

Claim 23 is currently pending under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claim 23 under 35 U.S.C. 112, first paragraph, is maintained for reasons of record advanced on pages 2-6 of the prior Office action, mailed 11/27/01 (Paper No. 7).

The claim as amended is directed to a method of treating myocardial failure in a human comprising administering an effective amount of transgene encoding for α-MHC, wherein said treatment provides improvement in left ventricular ejection fraction.

The specification discloses a method of myocardial gene therapy to increase α-MHC expression by delivering a transgene encoding α-MHC to a human so that the α-MHC transgene is expressed in the myocardial tissue of the heart (see p. 14, lines 20-28 of the instant application). The specification further discusses construction of the transgene (p.15 of the specification) and modes of delivery of the transgene (p, 16, lines 4-15 of the specification). The specification specifically

teaches up-regulation of α-MHC mRNA in myocardial tissue in human subjects suffering from cardiomyopathy, who received medical treatment with α-blocking agents (see example 5, of the instant application). It is reiterated that an increase in the amount of α-MHC mRNA in myocardial tissue does not provide a prediction of therapy for any subject having myocardial failure. Additionally, the specification fails to provide a correlation to therapeutic levels of expression of α-MHC transgenes in an *in vivo* setting in any subject having myocardial failure. Furthermore, the specification fails to teach or provide guidance for what level of α-MHC expression would provide a therapeutic effect in a human with myocardial failure, or how to measure the therapeutic effect in such a subject.

It is noted that the claim, as amended recites that the treatment provides an improvement in left ventricular ejection fraction. However, the specification fails to teach or show guidance for a correlation to therapeutic levels of expression of α-MHC transgenes *in vivo* such that improvement in the left ventricular ejection fraction would be improved. For reasons of record advanced in the prior Office actions, it is reiterated that the state of the art of gene therapy is unpredictable, and in particular, cardiovascular gene therapy is unpredictable. The specification fails to address how to overcome the unpredictabilities cited in the prior Office action, that are associated with the gene therapy art in general, and specifically as it pertains to the cardiovascular gene therapy. The rejection or question, in view of the guidance provided in the specification, is whether sufficient expression can be achieved by the exogenously administrated α–MHC DNA sequence to have any

effect of myocardial failure in a human, and in particular, the effect recited in the amended claim, that there would be an improvement in the left ventricular ejection fraction.

It is reiterated the Examiner's argument is directed to the unpredictable state of the gene therapy art, both in a general sense, and with particular regard to cardiovascular gene therapy, and furthermore, with particular regard to the expression of an α–MHC transgene; the Examiner's argument is not directed to the correlation of endogenous α-MHC expression with correlation to a disease-state phenotype. Furthermore, although Applicant provides an example of monitoring endogenous α–MHC mRNA levels *in vivo* to provide evidence to improved left ventricular ejection fraction, Applicant has not provided guidance or evidence to show a correlation to therapeutic levels of expression of α-MHC transgene expression in an *in vivo* setting in a subject suffering from myocardial failure; further, Applicant fails to show what levels of an α-MHC transgene expression are required to alleviate myocardial failure, or a protocol for reaching such levels

Thus it is maintained that the specification fails to enable the claimed invention for the reasons of record in the prior Office action (Paper No. 7) as discussed in the preceding paragraphs.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 23 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record advanced on pp. 6-7 of the prior Office action (Paper No. 7).

Claim 23 is incomplete. It is further unclear how the step of the method, "administering an effective amount of a transgene encoding α-MHC," correlates to the intended effect of the method (the preamble), "treating myocardial failure" since, in light of specification, mere administration of an α-MHC transgene would not be sufficient to achieve treatment of myocardial failure without the expression of the recombinant DNA. Amendment to the claim is requested.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thái-An N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to William Phillips, Patent Analyst, at (703) 305-3482. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

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